## REMARKS/ARGUMENTS

***Status of the Claims***

Upon entry of the present amendment, claims 1-7 and 14-22 are pending. New claims 14-22 are added, and claims 8-11 are canceled without prejudice to renewal.

New claim 14 sets forth a method of increasing the sensitivity of diagnosing Crohn's disease. Support is found, for example, on page 2, line 28 through page 3, line 9; and in Table 1 on page 7 where detection of the presence of IgA anti-OmpC antibodies increased the sensitivity of detection of the ASCA panel by an additional 20% and resulted in a cumulative detection sensitivity of 76%.

New claim 15 sets forth that the presence or absence of IgA anti-OmpC antibodies is detected in combination with detecting the presence or absence of antibodies against one or more microbial antigens other than OmpC associated with Crohn's disease. Support is found, for example, on page 2, line 28 through page 3, line 9; and in Table 1 on page 7.

Support for new claim 16 is found, for example, in originally filed claim 5 and in Table 1 on page 7.

New claims 17 and 18 set forth methods of diagnosing Crohn's disease by detecting the presence or absence of IgA anti-OmpC antibodies and IgA ASCA. Support is found, for example, in originally filed claims 1, 2 and 5, and in Table 1 on page 7.

New claim 19 finds support in originally filed claim 3.

New claim 20 finds support in originally filed claim 4.

New claim 21 finds support in originally filed claim 6.

New claim 22 finds support, for example, in Tables 1 and 2 on page 7.

***Restriction Requirement***

Applicants respectfully do not agree with the Examiner. However, in order to further prosecution of the present application, claims 8-11 have been canceled without prejudice to renewal. Applicants expressly reserve the right to prosecute the subject matter of claims 8-11 in a subsequently filed divisional application.

***Rejection under 35 U.S.C. § 112, first paragraph, enablement requirement***

In making this rejection, the Examiner has quoted the language of 35 U.S.C. § 112, second paragraph, but appears to make arguments based on the enablement requirement of 35 U.S.C. § 112, first paragraph.

The Examiner alleges that the presence of IgA anti-OmpC in about 55% of patients having Crohn's disease, as indicated in Table 2 of the specification, is not sufficient to establish adequate correlation between the presence of IgA anti-OmpC antibodies and the diagnosis of Crohn's disease. Table 2 also informs that anti-*Saccharomyces cerevisiae* antibodies (ASCA) are present in about 56% of patients in Crohn's disease, a percentage of Crohn's disease patients comparable to those having IgA anti-OmpC antibodies.

Sensitivity

The specification teaches that anti-*Saccharomyces cerevisiae* antibodies are a known differential marker for Crohn's disease for differentiating from ulcerative colitis (*see*, page 17, lines 19-23). Further, as shown in the attached published information from the Federal Register (Exhibit A) and from the Center for Devices and Radiological Health (Exhibit B), the United States Food and Drug Administration (FDA) recognizes detecting the presence or absence of ASCA as an aid in the diagnosis of Crohn's disease.[1] The FDA publications do not disclose or suggest that in order for detecting the presence or absence of ASCA to be useful in

[1] Exhibit A: 65 Fed. Reg. 70305-70307 (Nov. 22, 2000), "Immunology and Microbiology Devices; Classification of Anti-Saccharomyces cerevisiae (S. cerevisiae) Antibody (ASCA) Test Systems" (relevant passages highlighted); Exhibit B: "Class II Special Control Guidance Document for Anti-*Saccaromyces cervisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications," issued on August 23, 2000, (relevant passages highlighted) *both documents available through* www.fda.gov.

the diagnosis of Crohn's disease, the detection of further IgA antibodies for additional microbial antigens is necessary. The FDA publications represent the standard of those of skill in the art for the required prevalence of a particular microbial antigen in individuals having Crohn's disease for its use as an aid in the diagnosis of Crohn's disease. Because anti-*Saccharomyces cerevisiae* antibodies (ASCA) are present in a percentage of Crohn's disease patients comparable to those having IgA anti-OmpC antibodies, it follows that detecting the presence or absence of IgA anti-OmpC antibodies would also be recognized by the FDA as a useful aid in the diagnosis of Crohn's disease.

Specificity

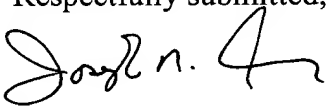
Detecting for the presence or absence of IgA anti-OmpC antibodies also provides an independent diagnostic marker for diagnosing the presence of Crohn's disease. This speaks to the specificity of the method. Whereas detecting for the presence of IgA anti-OmpC antibodies has a *sensitivity* of presence in about 55% of patients having Crohn's disease, the *specificity* of the method is measured differently. In a sample of about 28 individuals without Crohn's disease, only 1 tested positive for IgA anti-OmpC antibodies (*see*, Figure 4 and page 6, lines 4-11). The present method elicits very few falsely positive indications of Crohn's disease and therefore has a high *specificity*. Accordingly, when the presence of IgA anti-OmpC antibodies is detected, it is independently indicative that the patient has Crohn's disease.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Joseph R. Snyder
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
Attachments
JS:jlw
60409014 v2

# Exhibit A

**The Rule**

This action amends part 71 by establishing VOR Federal Airway V–457 in Alaska. Presently, there is an uncharted nonregulatory route using the same routings as the V–457 which becomes effective January 25, 2001. The FAA is establishing V–457 for the following reasons: (1) The conversion of this uncharted nonregulatory route to a VOR Federal airway adds to the IFR airway and route infrastructure in Alaska; (2) pilots will be provided with minimum en route altitudes and minimum obstruction clearance altitudes information; (3) this amendment establishes controlled airspace, thus eliminating some of the commercial IFR operations in uncontrolled airspace; and (4) the addition of this route improves the management of air traffic operations and thereby enhance safety.

The FAA has determined that this regulation only involves an established body of technical regulations for which frequent and routine amendments are necessary to keep them operationally current. Therefore, this regulation: (1) Is not a "significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and (3) does not warrant preparation of a regulatory evaluation as the anticipated impact is so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, it is certified that this rule, when promulgated, will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

Alaskan VOR Federal airways are published in paragraph 6010(b) of FAA Order 7400.9H dated September 1, 2000, and effective September 16, 2000, which is incorporated by reference in 14 CFR 71.1. The Alaskan VOR Federal airway listed in this document will be published subsequently in the order.

**List of Subjects in 14 CFR Part 71**

Airspace, Incorporation by reference, Navigation (air).

**The Rule**

In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

## PART 71—DESIGNATION OF CLASS A, CLASS B, CLASS C, CLASS D, AND CLASS E AIRSPACE AREAS; AIRWAYS; ROUTES; AND REPORTING POINTS

1. The authority citation for part 71 continues to read as follows:

**Authority:** 49 U.S.C. 106(g), 40103, 40113, 40120; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389.

**§ 71.1 [Amended]**

2. The incorporation by reference in 14 CFR 71.1 of Federal Aviation Administration Order 7400.9H, Airspace Designations and Reporting Points, dated September 1, 2000, and effective September 16, 2000, is amended as follows:

*Paragraph 6010(b) Alaskan VOR Federal Airways*

* * * * *

**V–457 [New]**

From Iliamna, AK, NDB; to Kenai, AK.

* * * * *

Issued in Washington, DC, on November 15, 2000.

**Reginald C. Matthews,**

*Manager, Airspace and Rules Division.*

[FR Doc. 00–29906 Filed 11–21–00; 8:45 am]

**BILLING CODE 4910–13–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

### 21 CFR Part 866

**[Docket No. 00N–1565]**

## Immunology and Microbiology Devices; Classification of Anti-Saccharomyces cerevisiae (S. cerevisiae) Antibody (ASCA) Test Systems

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is classifying the Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) test system into class II (special controls). The special control that will apply to this device is a guidance document entitled "Guidance for Industry and FDA Reviewers: Class II Special Control Guidance Document for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications." Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of this guidance document. The agency is taking this action in response to a petition submitted under the Federal Food, Drug, and Cosmetic Act (the act) as amended by the Medical Device Amendments of 1976, the Safe Medical Devices Act of 1990, and the Food and Drug Administration Modernization Act of 1997. The agency is classifying these devices into class II (special controls) in order to provide a reasonable assurance of the safety and effectiveness of the devices.

**DATES:** This rule is effective December 22, 2000.

**FOR FURTHER INFORMATION CONTACT:** Deborah M. Moore, Center for Devices and Radiological Health (HFZ–440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301–594–1293.

**SUPPLEMENTARY INFORMATION:**

### I. Background

In accordance with section 513(f)(1) of the act (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976, generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807 of the FDA regulations.

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) of the act for a device that has not previously been classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1) of the act, request FDA to classify the device under the criteria set forth in section 513(a)(1) of the act. FDA shall, within 60 days of receiving such a request, classify the device by written order. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** announcing such classification.

In accordance with section 513(f)(1) of the act, FDA issued an order on July 11, 2000, classifying the QUANTA Lite™ ASCA (*S. cerevisiae*) IgG ELISA in class III, because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. On July 18, 2000, FDA filed a petition submitted by INOVA Diagnostics, Inc., requesting classification of the QUANTA Lite™ ASCA (*S. cerevisiae*) IgG ELISA into class II under section 513(f)(2) of the act.

After review of the information submitted in the petition, FDA determined that the INOVA Diagnostics QUANTA Lite™ ASCA (*S. cerevisiae*) IgG ELISA can be classified in class II with the establishment of special controls. This device is intended for use in the semi-quantitative in vitro determination of anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibodies (ASCA) in human serum as an aid in the diagnosis of Crohn's disease. FDA believes that class II special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

In addition to the general controls of the act, the INOVA Diagnostics QUANTA Lite™ ASCA (*S. cerevisiae*) IgG ELISA is subject to a special control guidance document entitled "Guidance for Industry and FDA Reviewers: Class II Special Control Guidance for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications."

Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of this type of device and, therefore, the device is not exempt from the premarket notification requirements. The test is used in the diagnosis of Crohn's disease and FDA review of data sets and labeling ensure that minimum levels of performance are obtained before marketing and are subject to impartial external quality control before labeling is put into place. Thus, persons who intend to market this device must submit to FDA a premarket notification submission containing information on the anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) test system before marketing the device.

On August 16, 2000, FDA issued an order to the petitioner classifying the INOVA Diagnostics QUANTA Lite™ ASCA (*S. cerevisiae*) IgG ELISA, and substantially equivalent devices of this generic type, into class II under the generic name, anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) test system. FDA identifies this generic type of device as an anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) test system, which is intended to measure *Saccharomyces cerevisiae* (*S. cerevisiae*) antibodies (ASCA) in human serum or plasma as an aid in the diagnosis of Crohn's disease. FDA is codifying this device by adding § 866.5785. This order also identified a special control applicable to this device entitled "Guidance for Industry and FDA Reviewers: Class II Special Control Guidance for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications."

## II. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

## III. Analysis Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612) (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1996 (Public Law 104–121)), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4)). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so it is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. FDA knows of only one manufacturer of this type of device. Classification of these devices in class II will relieve this manufacturer of the device of the cost of complying with the premarket approval requirements of section 515 of the act (21 U.S.C. 360e) and may permit small potential competitors to enter the market place by lowering their costs. The agency, therefore, certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million in any one year (adjusted annually for inflation). The Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs and benefits for the final rule, because the final rule is not expected to result in any 1-year expenditure that would exceed $100 million.

## IV. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, or on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the order and, consequently, a federalism summary impact statement is not required.

## V. Paperwork Reduction Act of 1995

This final rule contains no collection of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

## List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is amended as follows:

## PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

1. The authority citation for 21 CFR part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 866.5785 is added to subpart F to read as follows:

**§ 866.5785 Anti-Saccharomyces cerevisiae (S. cerevisiae) antibody (ASCA) test systems.**

(a) *Identification.* The Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) test system is an in vitro diagnostic device that consists of the reagents used to measure, by immunochemical techniques, antibodies to *S. cerevisiae* (baker's or brewer's yeast) in human serum or plasma. Detection of *S. cerevisiae* antibodies may aid in the diagnosis of Crohn's disease.

(b) *Classification.* Class II (special controls). The special control is FDA's "Guidance for Industry and FDA Reviewers: Class II Special Control Guidance Document for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications."

Dated: November 9, 2000.

**Linda S. Kahan,**

*Deputy Director for Regulations Policy, Center for Devices and Radiological Health.*

[FR Doc. 00-29841 Filed 11-21-00; 8:45 am]

BILLING CODE 4160-01-F

## DEPARTMENT OF TRANSPORTATION

## Federal Highway Administration

## 23 CFR Part 645

**[FHWA Docket No. FHWA-99-6232]**

**RIN 2125-AE68**

## Utilities

**AGENCY:** Federal Highway Administration (FHWA), DOT.

**ACTION:** Final rule.

**SUMMARY:** The FHWA is issuing a final rule amending its regulation prescribing policies, procedures, and reimbursement provisions for the relocation and adjustment of existing utility facilities, and for the accommodation of new utility facilities and private lines on the right-of-way of Federal-aid and direct Federal highway projects. These amendments will bring the FHWA's utilities regulation into conformance with recent laws, regulations, or guidance, and will provide State transportation departments (STDs) clarification and more flexibility in implementing it.

**DATES:** This final rule is effective January 22, 2001.

**FOR FURTHER INFORMATION CONTACT:** Mr. Paul Scott, Office of Program Administration, HIPA-20, (202) 366-4104; or Mr. Reid Alsop, Office of the Chief Counsel, HCC-31, (202) 366-0791, Federal Highway Administration, 400 Seventh Street, SW., Washington, D.C. 20590-0001. Office hours are from 7:45 a.m. to 4:15 p.m., e.t., Monday through Friday, except Federal holidays.

**SUPPLEMENTARY INFORMATION:**

### Electronic Access

Internet users may access all comments received by the U.S. DOT Dockets, Room PL-401, by using the universal resource locator (URL): *http://dms.dot.gov.* It is available 24 hours each day, 365 days each year. Please follow the instructions online for more information and help.

An electronic copy of this document may be downloaded by using a modem and suitable communications software from the Government Printing Office's Electronic Bulletin Board Service at (202) 512-1661. Internet users may reach the Office of the Federal Register's home page at: *http://www.nara.gov/fedreg* and the Government Printing Office's database at: *http://www.access.gpo.gov/nara.*

### Background

The amendments in this final rule are based primarily on the notice of proposed rulemaking (NPRM) published at 65 FR 6344 on February 9, 2000 (FHWA Docket No. FHWA-99-6232). All comments received in response to this NPRM have been considered in adopting these amendments.

Present FHWA regulations regarding utility relocation and accommodation matters have evolved from basic principles established decades ago, with many of the policies remaining unchanged. The present regulations are found at 23 CFR part 645. Subpart A of this part pertains to utility relocations, adjustments, and reimbursement. Subpart B pertains to the accommodation of utilities.

The utility regulations were revised on May 15, 1985, when a final rule was published at 50 FR 20344. Three significant changes have occurred since then, on February 2 and July 1, 1988, when amendments to the regulation were published at 53 FR 2829 and 53 FR 24932; and on July 5, 1995, when a final rule was published at 60 FR 34846.

The February 2, 1988, amendment provided that each State must decide, as part of its utility accommodation plan, whether to allow longitudinal utility installations within the access control limits of freeways and if allowed under what circumstances.

The July 1, 1988, amendment clarified that costs incurred by highway agencies in implementing projects solely for safety corrective measures to reduce the hazards of utilities to highway users are eligible for Federal-aid participation.

The July 5, 1995, amendment eliminated the requirement for FHWA pre-award review and/or approval of consultant contracts for preliminary engineering; increased the ceiling for lump sum agreements from $25,000 to $100,000; clarified the meaning of the term "approved program" and the methodology to be used to compute indirect or overhead rates; required utilities to submit final billings within one year following completion of the utility relocation work; eliminated the certification of completed utility work and the requirement for evidence of payment prior to reimbursement; brought the definition of "clear zone" into conformance with the American Association of State Highway and Transportation Officials (AASHTO) "Roadside Design Guide"; and conformed the utilities regulations to the Intermodal Surface Transportation Efficiency Act of 1991 (ISTEA), Public Law 102-240, 105 Stat. 1914.

This final rule amends the regulation as follows:

- Incorporates an amendment conforming the utilities regulations to the Transportation Equity Act for the 21st Century (TEA-21), Public Law 105-178, 112 Stat. 107.
- Eliminates the $100,000 upper limit for lump-sum agreements.
- Allows reimbursement for utility relocations to be based upon unit costs.
- Clarifies the intent of the regulation requiring utilities to submit final billings within one year following completion of work.
- Deletes the provision encouraging STDs to adopt the alternate procedure for utilities.
- States that the most important consideration in determining whether a proposed facility is a utility or not, is how the STD views it under its own State laws and/or regulations.
- Eliminates a confusing provision to clarify the intent that the utility regulations are not applicable to longitudinal installations of private lines.

### Discussion of Comments

Interested persons were invited to participate in the development of this final rule by submitting written comments in response to the NPRM in Docket No. FHWA-99-6232 on or before April 10, 2000. Comments were received from 6 STDs and 1 utility company. A summary of the comments

# Exhibit B

Guidance for Industry and FDA Reviewers

# Class II Special Control Guidance Document for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications

**Document issued on: August 23, 2000**


**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Devices and Radiological Health**

**Immunology Branch**
**Division of Clinical Laboratory Devices**
**Office of Device Evaluation**

# Preface

## Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dr. Peter Maxim, Center for Devices and Radiological Health, HFZ-440, 2098 Gaither Road, Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Dr. Peter Maxim, (301) 594-1293.

## Additional Copies

World Wide Web/CDRH/home page at http://www.fda.gov/cdrh/ode/guidance/1183.pdf or CDRH Facts on Demand at 1-800-899-0381 or (301) 827-0111, 1183 when prompted for the document shelf number.

# Class II Special Control Guidance Document for Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) Premarket Notifications

***This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.***

## Background

On August 16, 2000, FDA classified Anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) Antibody (ASCA) *in vitro* diagnostic devices from Class III designation to Class II. This guidance document describes a means by which anti-*S. cerevisiae* antibody (ASCA) devices may comply with the requirements of class II special controls. Designation of this guidance document as a special control means that manufacturers of anti-*S. cerevisiae* antibody devices, who follow the recommendations listed in this document before introducing their device into commercial distribution in the United States, will be able to market their device after they have submitted a premarket notification submission, referred to as a 510(k), and received a finding of "substantial equivalence" for their device. Manufacturers should comply with either the recommendations of this guidance or some alternate means that provide equivalent assurance of safety and effectiveness.

## Scope

FDA identifies this generic type of device as an immunological device under 21 CFR §866.5785, product code NBT. This generic type of device, an anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) device is used for the semi-quantitative measurement of antibodies to *S. cerevisiae* (baker's and brewer's yeast) as an aid in the diagnosis of Crohn's disease.

## Risks to Health

FDA has identified two risks to health associated with this type of device. These risks involve: 1) a falsely elevated result leading to a medical decision causing a patient to undergo needless therapy or an unnecessary change in treatment; or 2) a

falsely low result delaying recognition by the physician of the presence or progression of disease causing treatment to be delayed.

## Special Controls Guidance

FDA believes the following controls, when combined with the general controls of the Food Drug and Cosmetic Act, will provide reasonable assurance of the safety and effectiveness of this type of device: labeling, design controls, and clinical information.

1. The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR §801.109.

2. Labeling in accordance with 21 CFR §809.10 (b). In addition, labeling should:

    a. support statements throughout the document with literature citations
    b. include an intended use statement with test methodology, specimen type, and whether the assay is qualitative or semi-quantitative
    c. include a summary of results from the clinical studies
    d. include quality control recommendations
    e. give an adequate description of the interpretation of results and expected results (incidence of ASCA in normal and diseased populations)
    f. include special limitations of the assay, e.g. restrictions in the pediatric population; the significance of a positive or negative result; use of the stated sample matrix only; etc.

3. Clinical information in the submission should demonstrate:

    a. the sensitivity in the target population
    b. specificity in other gastrointestinal disease and in healthy, non-diseased groups
    c. incidence of ASCA in all groups studied

4. Analytical/Laboratory performance studies should include:

    a. validation of the cut-off
    b. prevalence in the asymptomatic population
    c. assay specificity/interfering substances
    d. reproducibility at the cut-off and over the reportable range of the assay

e. antigen characterization
f. method and reagent description

5. Copies of current literature to support the use of ASCA in the diagnosis of Crohn's disease

For additional information refer to the following FDA guidance documents:

- Review Criteria for Assessment of Anti-Nuclear Antibodies (ANA) *in vitro* Diagnostic Devices Using Indirect Immunofluorescence Assay (IFA) Immunodiffusion (IMD) and Enzyme-Linked Immunosorbent Assay (ELISA) at http://www.fda.gov/cdrh/ode/848.pdf

- Review Criteria for Assessment of Rheumatoid Factor (RF) *in vitro* Diagnostic Devices Using Enzyme-Linked Immunoassay (EIA) Enzyme-Linked Immunosorbent Assay (ELISA) Particle Agglutination Tests and Laser and Rate Nephelometry at http://www.fda.gov/cdrh/ode/rhuema.html.

- Review Criteria for *in vitro* Diagnostic Devices for the Assessment of Thyroid Autoantibodies Using Indirect Immunofluorescence Assay (IFA), Indirect Hemagglutination Assay (IHA), Radioimmunoassay (RIA), and Enzyme-Linked Immunosorbent Assay (ELISA) at http://www.fda.gov/cdrh/ode/odecl051.html.

These documents are available on the Internet as shown or from the Division of Small Manufacturers Assistance at its toll-free number (800) 899-0381 or (301) 827-0111

## Premarket Notification

FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of this generic type of device, and therefore, the device type is not exempt from the premarket notification requirements. Thus, persons who intend to market a device of this type need to submit a premarket notification to FDA and receive agency clearance prior to marketing the device.